ulcers within 10 weeks, the diagnosis of anorectal ergotism can be assumed on clinical grounds.

The prognosis seems to depend on the time of diagnosis and the severity of ergotamine abuse. In our first case, with a particularly longstanding and excessive overdosage, severe fibrosis and incontinence developed. Höchter *et al.*[6] described a case of 15 years' abuse with consequent rectovaginal fistula and circular fibrosis. The latter may be the result of a further specific action of ergotamine beyond chronic inflammation, because various forms of fibrosis such as retroperitoneal, pleuropulmonary and pericardial fibrosis have been reported following longstanding overdosage of ergotamine[3,17]. Apart from these severe cases, complete restitution can be expected in most cases of anorectal ulcers due to migraine suppositories.

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Severe symptomatic hypoglycaemia due to quinine therapy

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Keywords: hypoglycaemia, quinine, insulin, B-cell

Hypoglycaemia due to quinine therapy occurs in the treatment of malaria[1] and an asymptomatic case has been reported following treatment for muscle cramp[2]. We report a case of severe persistent hypoglycaemia in a patient with terminal renal failure who had been treated for muscle cramp with quinine. The findings accord with the hypothesis that quinine causes inappropriate insulin release by the pancreatic beta-cell.

Case report

A 72-year-old woman was admitted in hypoglycaemic coma (blood glucose <1.0 mmol/l) which responded immediately to infusion of 50 ml 50% dextrose. Seven years previously she had undergone left mastectomy for poorly differentiated adenocarcinoma of the breast and three months before had developed a recurrence with subcutaneous metastases. For three days she had suffered anorexia and severe muscle cramps and had become anuric. Her therapy for several months had comprised ibuprofen 200 mg three times daily, with lorazepam 1 mg and quinine sulphate 300 mg taken at night. There was no past history or family history of diabetes mellitus. Neither the patient nor any family member had been treated with or had access to insulin or oral hypoglycaemic agents.

On examination she had a large pelvic mass. Blood urea was 47.4 mmol/l and creatinine 1730 mmol/l, and a diagnosis of renal failure due to ureteric obstruction was made. Details of other biochemical measurements are given in Table 1.

For the seven days until she died continuous intravenous infusion of dextrose was required to prevent recurrent hypoglycaemia. At post-mortem widespread metastatic breast cancer with bilateral ureteric obstruction was confirmed. The adrenals were partially replaced by metastases but the pancreas appeared normal. Immunohistology using guinea-pig antibodies to human insulin and glucagon (Dakopatts, Santa Barbara, California, USA) demonstrated the presence and normal distribution of these hormones in the pancreas. In contrast, neither hormone was identified in the breast carcinoma. Hepatic glycogen stores were exhausted.

Discussion

Spontaneous hypoglycaemia is an uncommon condition. It has been reported in patients with end-stage renal failure but the causal mechanism is

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Table 1. Plasma hormone, metabolite and quinine levels

	Glucose (mmol/l)	*Insulin (mU/l)*	*C-peptide (nmol/l)*	*Lactate (mmol/l)*	*Ketones (mmol/l)*	*Quinine (mg/l)*	*Cortisol (nmol/l)*
On admission	0.8	10.3	0.8	—	—	—	655
After 50 ml 50% dextrose	15.1	34.8	1.7	1.14	0	8.75	545
During glucose infusion 1 day post-admission	10.0	14.9	1.7	—	—	8.00	—
Fasted 4 days post-admission	1.7	2.1	0.3	1.03	0	—	770
Normal ranges	3.5–5	5.0± 2.6●	0.37± 0.14●	0.6–1.2	<0.3●	—	330–770

● Fasting.

uncertain[3]. It has been ascribed to loss of gluconeogenic substrate supply in the form of alanine normally released from the kidney[4], but hypoglycaemia can occur when adequate amounts of substrates are available[5]. Similarly, insulin clearance is reduced in renal failure but insulin concentrations do not rise[6] and raised insulin concentrations have not been reported in patients with hypoglycaemia[5].

In this patient the severe symptomatic hypoglycaemia was associated with elevated plasma insulin concentrations and low blood ketone body concentrations, indicating inappropriate secretion of insulin (Table 1). The failure of the tumour to stain for insulin and the parallel increase in C-peptide concentrations exclude the possibility of ectopic hormone secretion[7] and suggest a pancreatic source for the hormone.

That glycogen had not accumulated in the liver despite glucose infusion indicates that peripheral glucose consumption was rapid. The lack of hepatic glycogen may have contributed to the severity of the hypoglycaemia since it would have attenuated any counter-regulatory response, e.g. to the elevated cortisol concentrations (Table 1). It may also explain why hypoglycaemia was observed on the fourth day after admission when the plasma insulin concentration was not markedly elevated, though still sufficiently high to inhibit ketogenesis. Unfortunately, the plasma quinine concentration was not measured at this time.

The presence of the tumour *per se* is unlikely to have contributed to the hypoglycaemia. Hypoglycaemia due to breast carcinoma has not been described[8] and is typically caused by tumours of mesenchymal and not epidermal origin[9]. Tumours causing hypoglycaemia characteristically metabolize large amounts of glucose to lactate anaerobically[10,11], as do red blood cells parasitized by malarial plasmodia[12]. The basal blood lactate concentration was not elevated in this patient (Table 1), unlike the cases with malaria[1], and did not increase with glucose infusion, in contrast to metabolically active sarcomas[13]. This indicates either that tumour glycolysis was not very active or that excess lactate was being fully reconverted to glucose by hepatic gluconeogenesis via the Cori cycle[14].

The plasma concentrations of quinine were comparable to those found in cases of malaria receiving 600 mg of quinine 8-hourly[1], six times the dose administered to this patient. Quinine is normally excreted via the kidneys and the high plasma concentrations reflect drug accumulation due to renal failure.

Insulin release from isolated pancreatic islets of Langerhans is stimulated by quinine *in vitro*[15]. It augments the insulinotropic effect of glucose and also stimulates the release of insulin at low glucose concentrations, probably through the activation of voltage-sensitive calcium channels by inhibition of potassium conductance[16]. We suggest, therefore, that the inappropriate beta-cell secretion of insulin was due to the accumulated dose of quinine.

This case supports other evidence that quinine can cause inappropriate insulin release leading to symptomatic hypoglycaemia. Quinine is widely prescribed, and often regarded, wrongly, as a trivial medication. Whether it can precipitate hypoglycaemia by augmenting the action of oral hypoglycaemic agents remains to be determined, but its use should be suspected as a contributory factor in patients presenting with hypoglycaemia, particularly in those with renal impairment.

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Meningococcal septicaemia presenting as drug hypersensitivity

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Keywords: Acute vasculitis, hypersensitivity reaction, arthralgia, retinal detachment

A case is reported of meningococcal septicaemia presenting as an acute vasculitis without any features of meningitis. Hypersensitivity reactions to drugs commonly present as an acute vasculitis and may require treatment with corticosteroids. Even when clinical and microbiological features of infection and meningitis are absent, it is wise to combine steroid therapy for acute vasculitis with an antibiotic.

Case report

A 60-year-old housewife was admitted with an acute onset of severe widespread arthralgia. The previous day she had developed a red rash on her arms, mild fever and malaise and a red painless injected eye. There was no loss of vision, photophobia or headache.

Nine months previously she had been treated for osteoarthrosis with fenbufen. She had taken 2 tablets for several days prior to this admission. Her only other therapy was thyroxine 0.1 mg daily for hypothyroidism following treatment of thyrotoxicosis with radioiodine in 1980.

On examination she was apyrexial, pulse 80 per minute, blood pressure 140/70 mmHg. There was a purpuric vasculitic rash affecting the limbs and conjunctival injection in the right eye. The fundi, pupil reactions and vision were normal. All limb joints were tender with painful limitation of movement but there were no effusions or soft tissue swelling. She had widespread muscle tenderness and weakness that was more marked distally. There was no neck stiffness and Kernig's sign was negative.

Investigations were as follows: Hb 11.9 g/dl, WBC 19.4×10^9/l (97% neutrophils, 3% lymphocytes), platelets and clotting times normal; ESR 105 mm/h, ASOT, antinuclear factor and rheumatoid factor were negative and complement levels were normal. An electromyogram showed patchy excess of short polyphasic units indicating a myopathic lesion and serum creatinine phosphokinase levels were elevated at 399 iu (normal range 0–200). Initial blood cultures ×6, throat and nose swabs ×3 and gonococcal complement fixation tests were all negative.

Over the next two days she developed a pyrexia of 39°C and was increasingly unwell. Since numerous bacteriological cultures were all negative, it was felt she had a hypersensitivity reaction to fenbufen and she was commenced on prednisolone 30 mg daily. Her temperature fell and the rash began to resolve. However, muscle weakness and tenderness persisted. Eight days after admission she awoke with a totally blind, painless left eye. The vitreous was opaque so that the fundus could not be seen. Intraocular pressure was low. Blood cultures and nose and throat swabs were repeated. The dose of oral prednisolone was increased to 80 mg daily. In addition she was treated with local dexamethasone 0.1%, cyclopentolate 1% and atropine 1% eye drops.

Six days later and two weeks after admission, blood cultures grew *Neisseria meningitidis*. The organism was also cultured from nose and throat swabs which had initially been clear. She was commenced on erythromycin and continued to take prednisolone 80 mg daily. Within three days the cutaneous vasculitis and arthralgia had resolved. Antibiotics were continued for two weeks and the dose of steroids was gradually reduced. Four weeks after admission the myopathy had totally resolved. She was referred to Moorfields Hospital (Mr Peter Leaver) where a diagnosis of retinal detachment secondary to vitreous collapse was made and the retinal detachment was repaired. The vision in her left eye gradually improved.

Discussion

The fact that many patients who have a meningococcal infection do not have meningitis is well recognized[1]. This patient did not have neck stiffness or photophobia and there were no other signs of meningism. Since her illness had all the features of an allergic vasculitis following ingestion of fenbufen, she was commenced on steroid therapy. Six initial blood cultures did not grow *N. meningitidis* and it was only when steroid treatment was started that they became positive. It seems probable, therefore, that steroid therapy precipitated the development of a florid bacteraemia. The illness rapidly resolved when antibiotics were commenced.

Vitreous collapse may occur in any septicaemia. The sudden onset of loss of vision in this case was in keeping with a retinal detachment secondary to vitreous collapse. In generalized meningococcal disease inflammatory reactions may occur in nearly all organs[2]. It is thought that skin lesions could be due to the Schwartzman reaction[3]. Circulating immune complexes have been demonstrated in severe cases of meningococcal infection[4]. Such patients require treatment with steroids in addition to antibiotics.

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